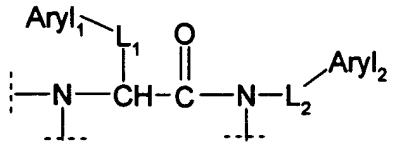
Claims

We Claim:

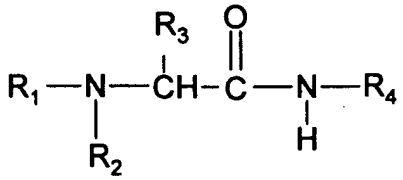
1. A compound comprising at least one moiety of the formula



wherein L_1 and L_2 are each a hydrocarbon group of from 1 to 6 carbons or a direct bond, and $Aryl_1$ and $Aryl_2$ are aryl, wherein each of $Aryl_1$ and $Aryl_2$ are substituted by at least one lipophilic group.

2. The compound of Claim 1, wherein the lipophilic group is selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylaryl, or C_1-C_6 alkoxyaryl.

3. A compound of Formula (I):



(I)

wherein

R_1 and R_2 are independently selected from

a) –H;

b) -C_{1-6} alkyl;

c) –aryl;

d) -C_{1-6} alkylaryl;

e) -C(O)-O-C_{1-6} alkyl;

f) -C(O)-O-C_{1-6} alkylaryl;

g) -C(O)-NH-C_{1-6} alkyl;

h) -C(O)-NH-C_{1-6} alkylaryl;

i) -SO_2-C_{1-6} alkyl;

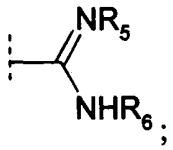
j) -SO_2-C_{1-6} alkylaryl;

k) -SO_2-aryl;

l) -SO_2-NH-C_{1-6} alkyl;

m) -SO_2-NH-C_{1-6} alkylaryl;

n)



;

o) -C(O)-C_{1-6} alkyl; and

p) -C(O)-C_{1-6} alkylaryl;

R_3 is selected from

a) -C_{1-6} alkyl;

b) –aryl; and

c) -C_{1-6} alkylaryl;

R_4 is selected from

a) -C_{1-6} alkylaryl;

b) -C_{1-6} alkoxyaryl; and

c) –aryl;

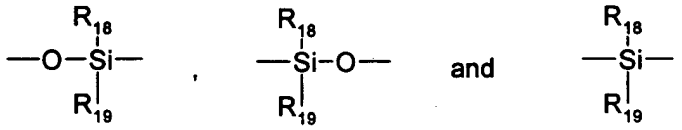
R_5 and R_6 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylaryl, and aryl; and wherein

the aryl and/or alkyl group(s) in R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{18}, R_{19}, and R_{20} may be optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{-1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,



and

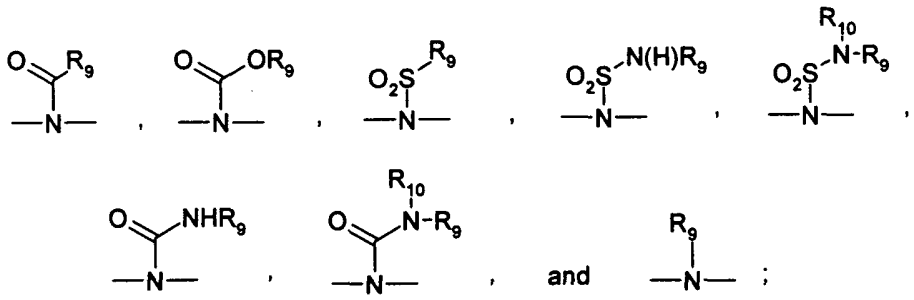
c) halogen, hydroxyl, cyano, carbamoyl, or carboxyl; and

R_{18} and R_{19} are independently selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl;

R_7, R_8, R_9 and R_{10} are independently selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl; and wherein

R_7 and R_8 may be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atom to which R_7 and R_8 are attached, and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m and n are, independently, 1, 2, 3, or 4; X is selected from the group consisting of $-CH_2-$, -O-, -S-, $-S(O_2)-$, -C(O)-, -CON(H)-, $-NHC(O)-$, $-NHCON(H)-$, $-NHSO_2-$, $-SO_2N(H)-$, $-C(O)-O-$, $-O-C(O)-$, $-NHSO_2NH-$,



or a pharmaceutically acceptable salt, solvate or prodrug thereof.

4. The compound of claim 3, wherein:

R_1 is hydrogen;

R_2 is selected from

a) -H;

b) $-C_{1-6}$ alkyl;

c) $-C_{1-6}$ alkylaryl;

d) $-C(O)-O-C_{1-6}$ alkyl;

e) $-C(O)-NH-C_{1-6}$ alkyl;

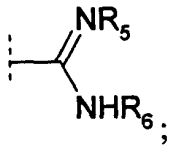
f) $-C(O)-NH-C_{1-6}$ alkylaryl;

g) $-SO_2-C_{1-6}$ alkyl;

h) $-SO_2-C_{1-6}$ alkylaryl;

i) $-SO_2-NH-C_{1-6}$ alkyl; and

j)



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k) -C(O)-C_{1-6} alkyl;

l) -C(O)-C_{1-6} alkylaryl;

R_3 is selected from

a) -C_{1-4} alkylaryl; and

R_4 is selected from

a) -C_{1-6} alkylaryl; and

b) –aryl;

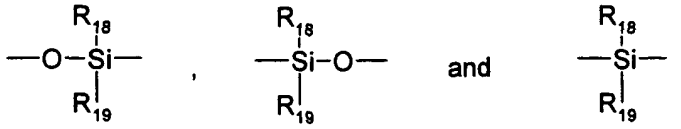
and wherein the aryl group in R_1, R_2, R_3 and R_4 is optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{-1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-,

-NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -$SO_2N(H)$-, -C(O)-O-, -$NHSO_2NH$-, -O-CO-,



and

c) halogen, hydroxyl, carbamoyl, and carboxyl;

R_{18} and R_{19} are selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, or C_1-C_6 alkylaryl, and wherein

R_7 and R_8 are selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, or C_1-C_6 alkylaryl; and wherein

R_7 and R_8 may be taken together to form a ring having the formula -$(CH_2)_m$-X-$(CH_2)_n$- bonded to the nitrogen atom to which R_7 and R_8 are attached, and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula -$(CH_2)_m$-X-$(CH_2)_n$- bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m, n, and X are as defined in claim 3.

5. The compound of claim 3, wherein R_3 is C_{1-3} alkylaryl and R_4 is aryl.

6. The compound of claim 5, wherein the aryl is substituted with -Y-C_{-1-6} alkylaryl.

7. The compound of claim 3, wherein R_2 is –C(O)-O-C_{1-6} alkyl.

8. The compound of claim 3, wherein R_3 is C_{1-3} alkylaryl, said aryl optionally substituted by substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

-Y-C_{1-6} alkyl;

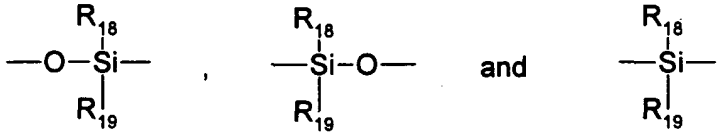
-Y-aryl;

-Y-C_{-1-6} alkylaryl;

-Y-C_{1-6}-alkyl-NR_7R_8; and

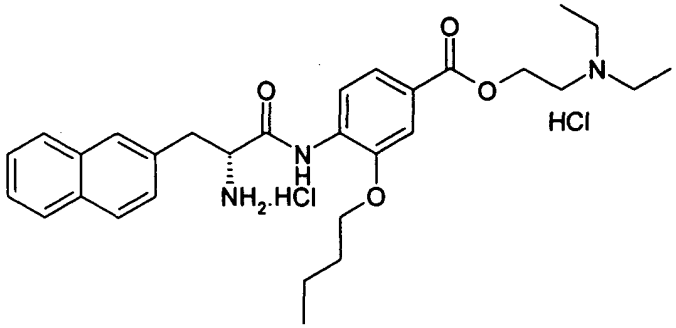
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,



9. The compound of claim 8, wherein aryl is phenyl or napthyl, optionally substituted by C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylaryl, or C_{1-6} alkoxyaryl.

10. The compound of claim 3, wherein said compound is selected from the group consisting of compounds of the following formulae:



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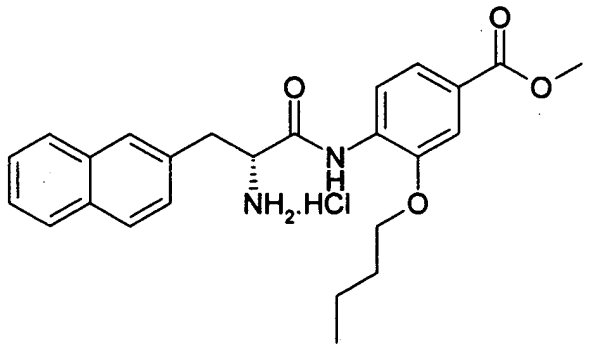

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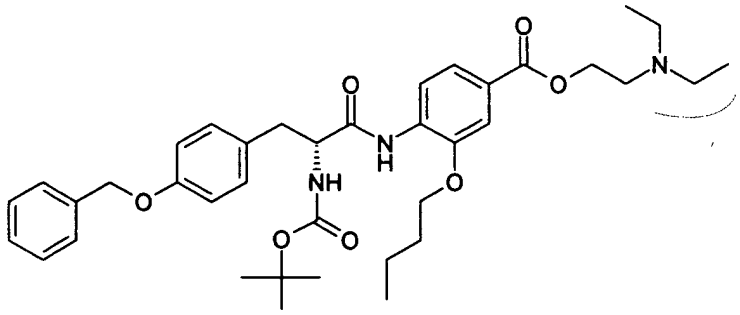

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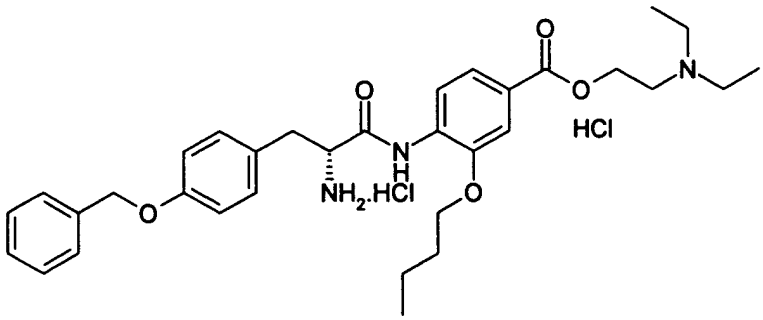

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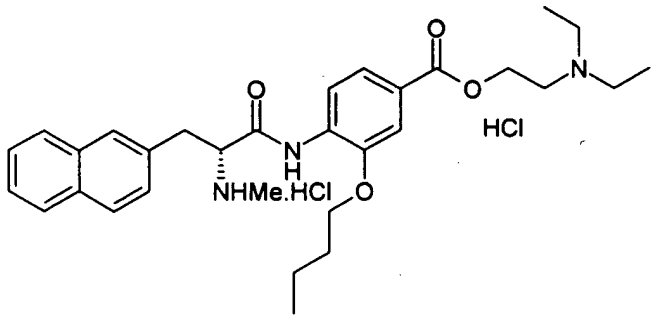

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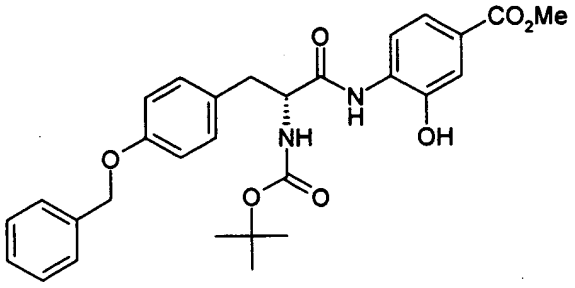
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OH
NH
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O
O

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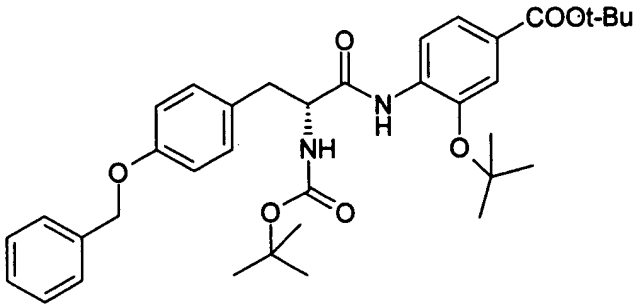
COOt-Bu
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N
H
NH
O
O
O
O

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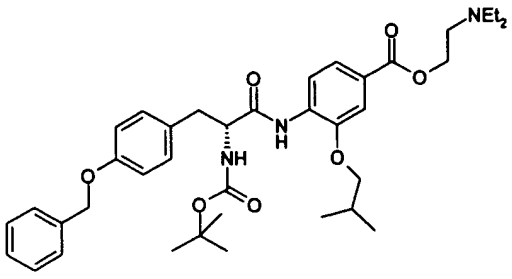
NEt2
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O
N
H
NH
O
O
O

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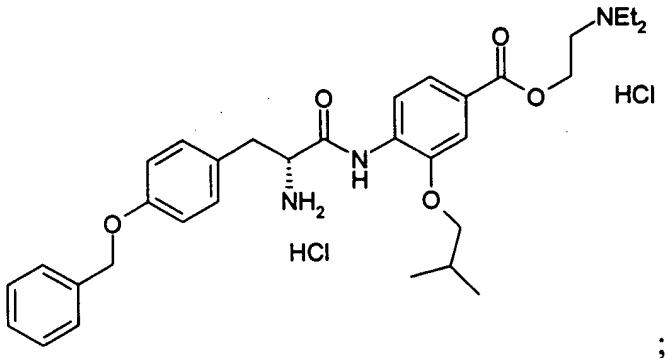
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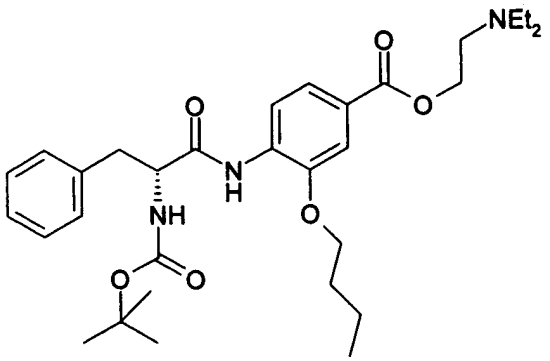
HCl
O
N
H
NH2
HCl
O

;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O
O
N
H
NH
O
O
O

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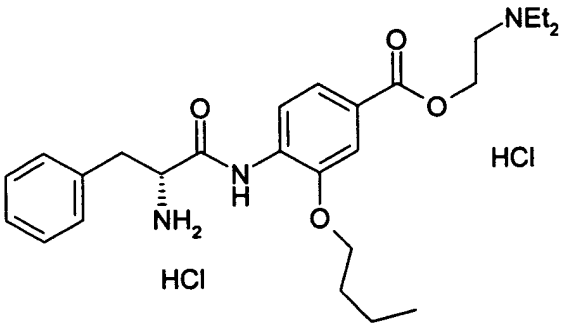
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O
N
H
NH2
O
HCl
HCl

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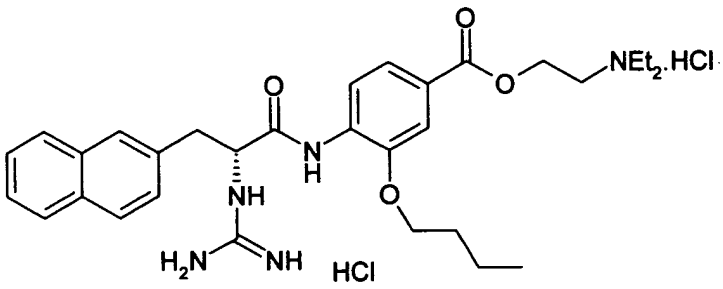
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O
NEt2.HCl
N
H
NH
O
H2N
NH
HCl

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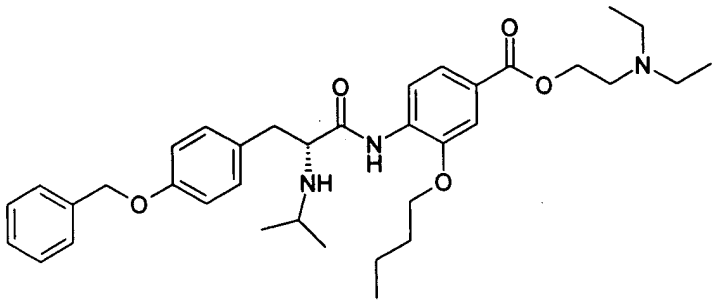
O
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N
O
N
H
NH
O

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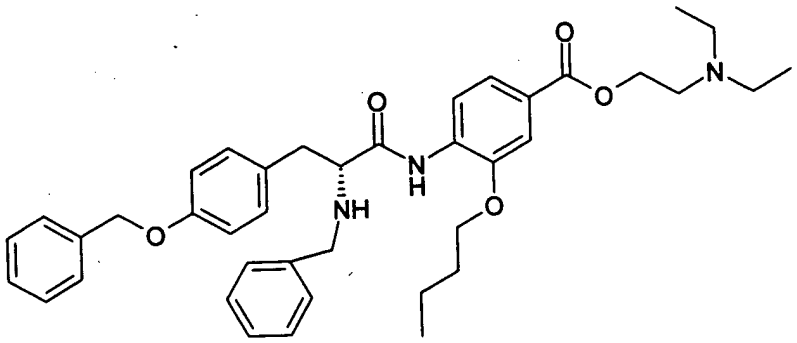

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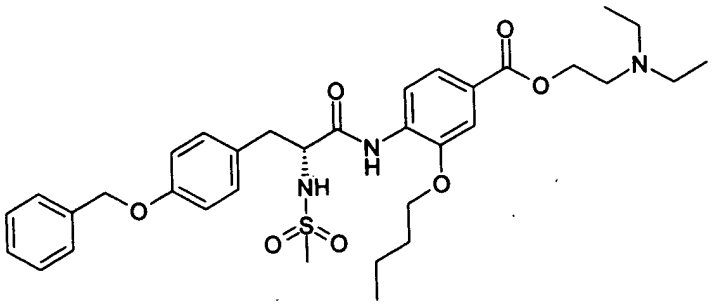

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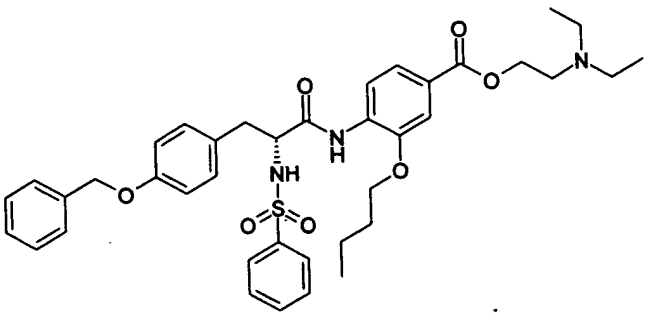

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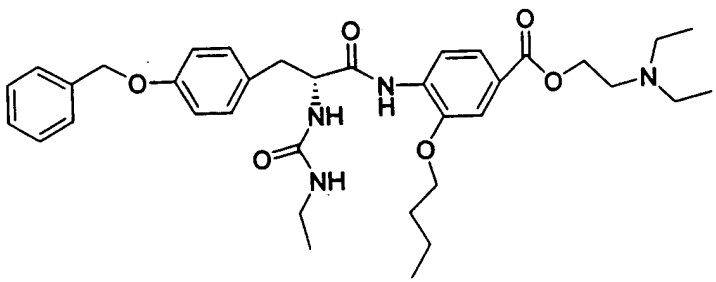

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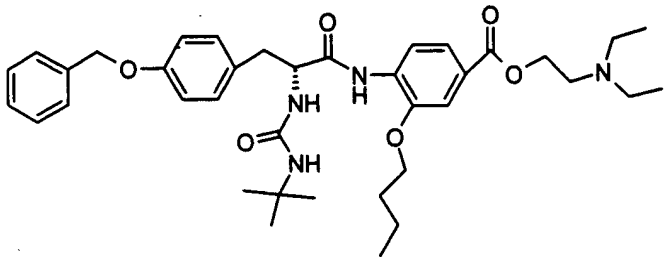

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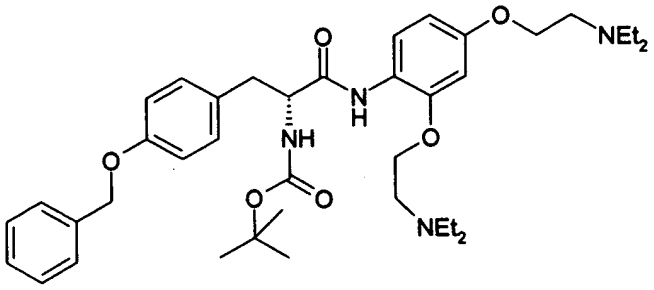

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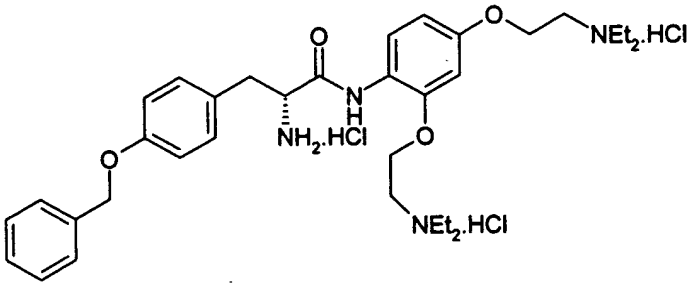

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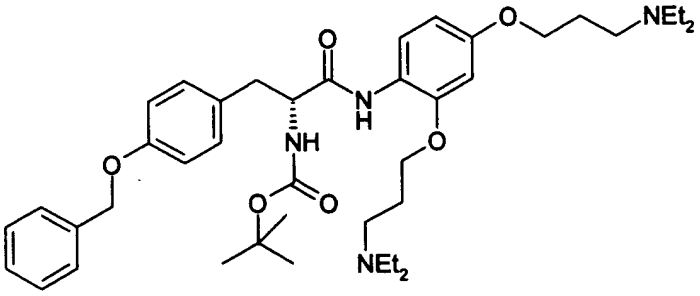

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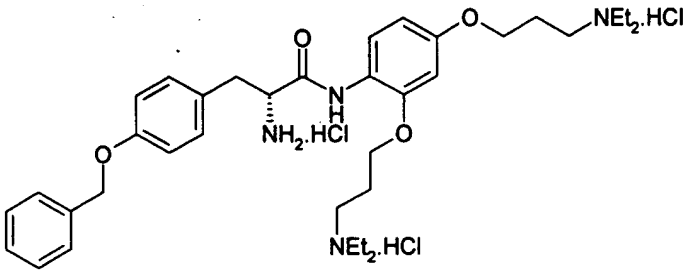
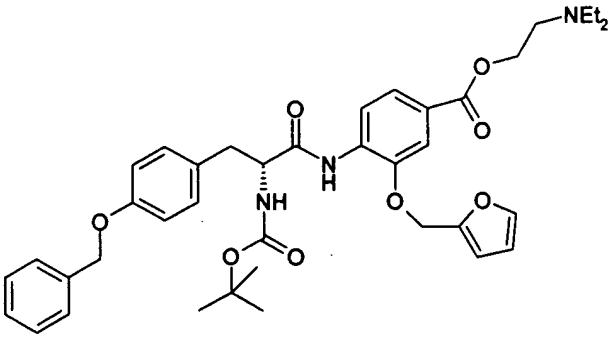

NEt2.HCl
O
N
H
NH2.HCl
O
O
NEt2.HCl

;


NEt2
O
O
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N
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NH
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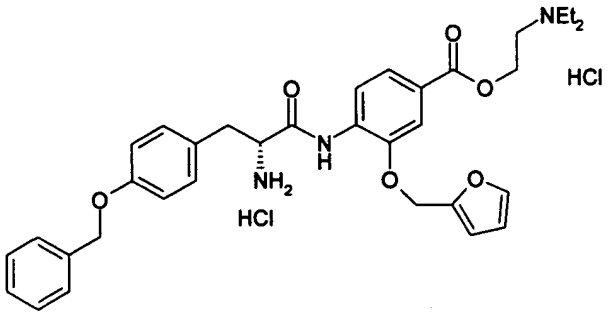
NEt2
HCl
O
O
O
N
H
NH2
HCl
O
O

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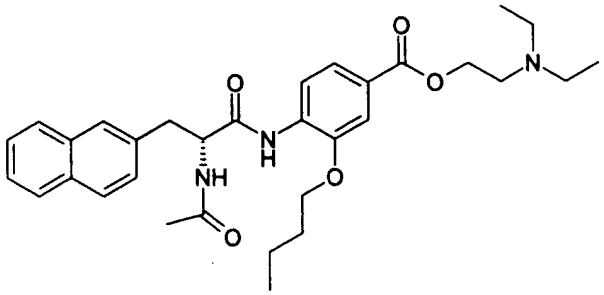
O
O
N
H
O
N
NH
O
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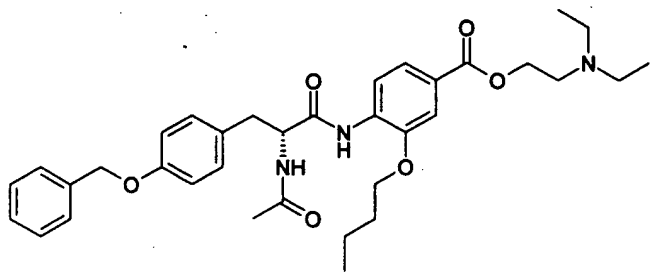
; and



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or the free amine, free acid, solvate, prodrug, or pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition comprising a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents.

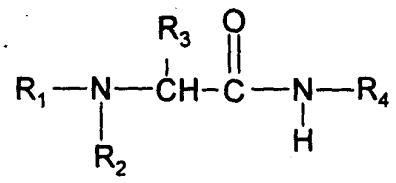
12. The pharmaceutical composition of to claim 11, in the form of an oral dosage or parenteral dosage unit.

13. The pharmaceutical composition of claim 11, wherein said compound is administered as a dose in a range from about 0.01 to 500 mg/kg of body weight per day.

14. The pharmaceutical composition of claim 11, wherein said compound is administered as a dose in a range from about 0.1 to 200 mg/kg of body weight per day.

15. The pharmaceutical composition of claim 11, wherein said compound is administered as a dose in a range from about 0.1 to 100 mg/kg of body weight per day.

16. A pharmaceutical composition comprising compound of Formula (I):



(I)

wherein

R_1 and R_2 are independently selected from

a) –H;

b) -C_{1-6} alkyl;

c) –aryl;

d) -C_{1-6} alkylaryl;

e) -C(O)-O-C_{1-6} alkyl;

f) -C(O)-O-C_{1-6} alkylaryl;

g) -C(O)-NH-C_{1-6} alkyl;

h) -C(O)-NH-C_{1-6} alkylaryl;

i) -SO_2-C_{1-6} alkyl;

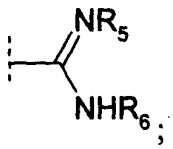
j) -SO_2-C_{1-6} alkylaryl;

k) -SO_2-aryl;

l) -SO_2-NH-C_{1-6} alkyl;

m) -SO_2-NH-C_{1-6} alkylaryl;

n)



;

o) -C(O)-C_{1-6} alkyl; and

p) -C(O)-C_{1-6} alkylaryl;

R_3 is selected from

a) -C_{1-6} alkyl;

b) –aryl; and

c) -C_{1-6} alkylaryl;

R_4 is selected from

a) -C_{1-6} alkylaryl;

b) -C_{1-6} alkoxyaryl; and

c) –aryl;

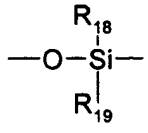
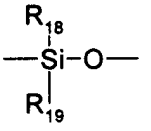
R_5 and R_6 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylaryl, and aryl; and wherein

the aryl and/or alkyl group(s) in R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{18}, R_{19}, and R_{20} may be optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,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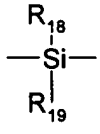

; and

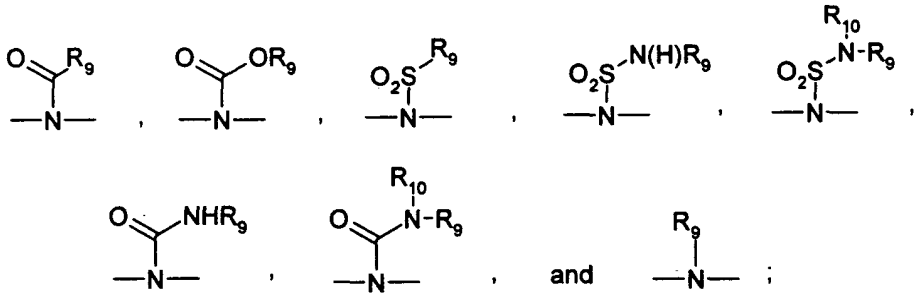
c) halogen, hydroxyl, cyano, carbamoyl, or carboxyl; and

R_{18} and R_{19} are independently selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl;

R_7, R_8, R_9 and R_{10} are independently selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl; and wherein

R_7 and R_8 may be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atom to which R_7 and R_8 are attached, and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m and n are, independently, 1, 2, 3, or 4; X is selected from the group consisting of $-CH_2-$, -O-, -S-, $-S(O_2)-$, -C(O)-, -CON(H)-, -NHC(O)-, -NHCON(H)-, $-NHSO_2-$, $-SO_2N(H)-$, -C(O)-O-, -O-C(O)-, $-NHSO_2NH-$,



or a pharmaceutically acceptable salt, solvate or prodrug thereof; and one or more pharmaceutically acceptable carriers, excipients, or diluents.

17. The composition of claim 16, wherein:

R_1 is hydrogen;

R_2 is selected from

a) -H;

b) -C_{1-6} alkyl;

c) -C_{1-6} alkylaryl;

d) -C(O)-O-C_{1-6} alkyl;

e) -C(O)-NH-C_{1-6} alkyl;

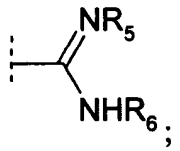
f) -C(O)-NH-C_{1-6} alkylaryl;

g) -SO_2-C_{1-6} alkyl;

h) -SO_2-C_{1-6} alkylaryl;

i) -SO_2-NH-C_{1-6} alkyl; and

j)



;

k) -C(O)-C_{1-6} alkyl;

l) -C(O)-C_{1-6} alkylaryl;

R_3 is selected from

a) -C_{1-4} alkylaryl; and

R_4 is selected from

a) -C_{1-6} alkylaryl; and

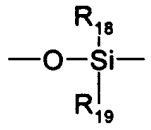
b) –aryl;

and wherein the aryl group in R_1, R_2, R_3 and R_4 is optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{-1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,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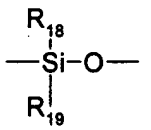
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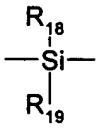

;
and

c) halogen, hydroxyl, carbamoyl, and carboxyl;

R_{18} and R_{19} are selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, or C_1-C_6 alkylaryl, and wherein

R_7 and R_8 are selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, or C_1-C_6 alkylaryl; and wherein

R_7 and R_8 may be taken together to form a ring having the formula -$(CH_2)_m$-X-$(CH_2)_n$- bonded to the nitrogen atom to which R_7 and R_8 are attached, and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula -$(CH_2)_m$-X-$(CH_2)_n$-

bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m, n, and X are as defined in claim 16.

18. The composition of claim 16, wherein R_3 is C_{1-3} alkylaryl and R_4 is aryl.

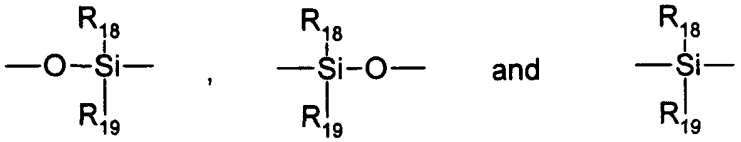
19. The composition of claim 18, wherein the aryl is substituted with -Y-C_{1-6} alkylaryl.

20. The composition of claim 16, wherein R_2 is –C(O)-O-C_{1-6} alkyl.

21. The composition of claim 16, wherein R_3 is C_{1-3} alkylaryl, said aryl optionally substituted by substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

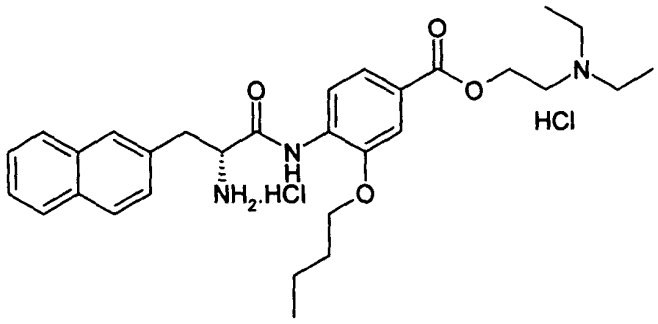
-Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,



22. The composition of claim 21, wherein aryl is phenyl or napthyl, optionally substituted by C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylaryl, or C_{1-6} alkoxyaryl.

23. The composition of claim 16, wherein said compound is selected from the group consisting of compounds of the formulae:



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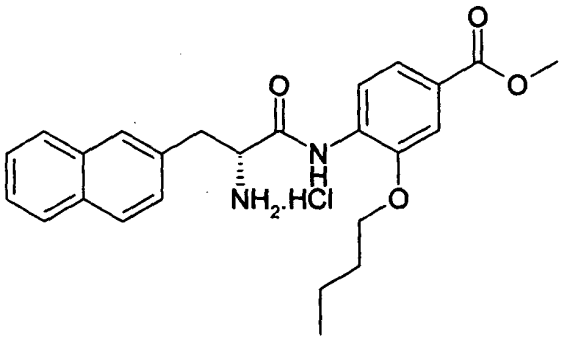

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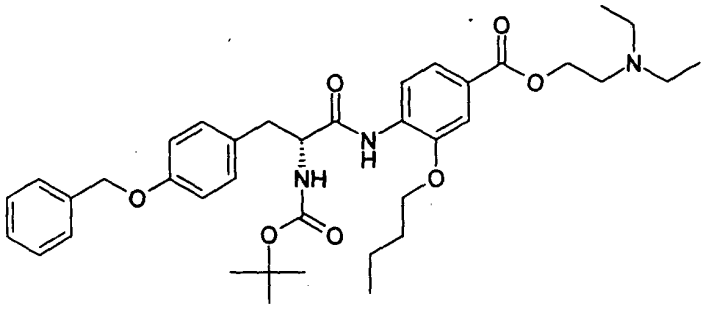

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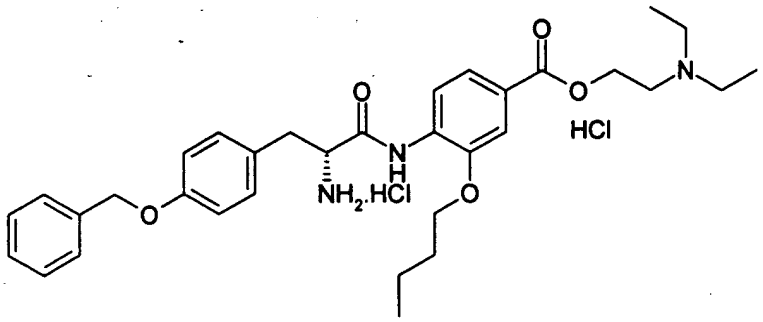
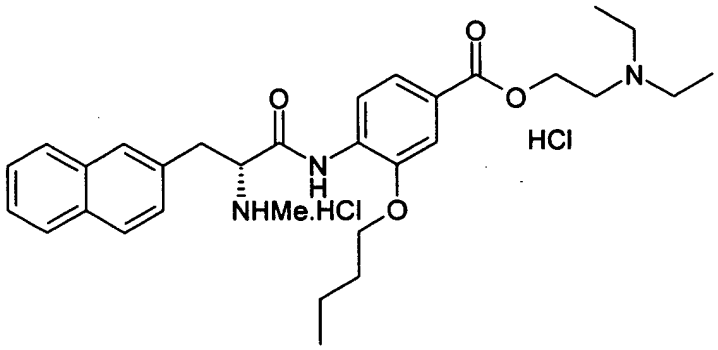
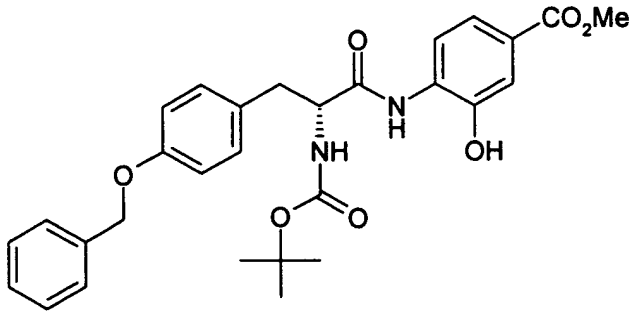

O
O
N
HCl
O
O
N
H
NH2.HCl
O

;


O
O
N
HCl
O
N
H
NHMe.HCl
O

;


CO2Me
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N
H
NH
OH
O
O
O

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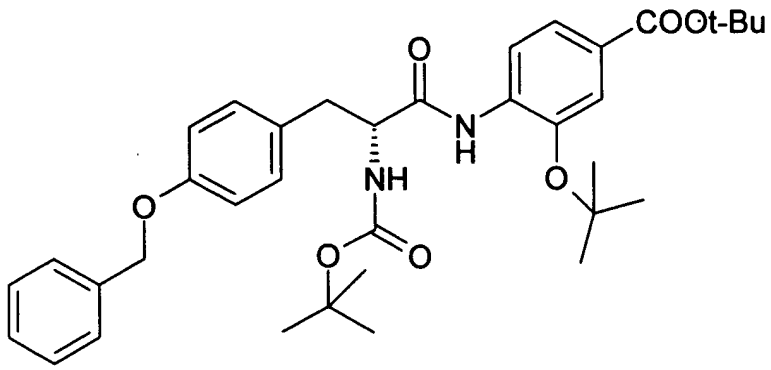
COOt-Bu
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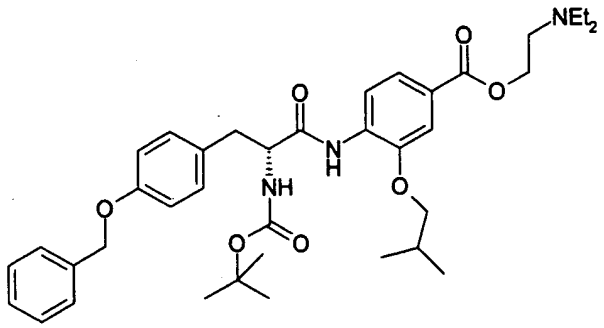
N
H
NH
O
O
O
O

;



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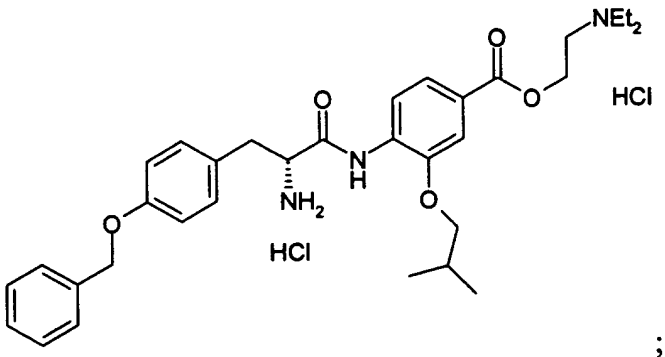

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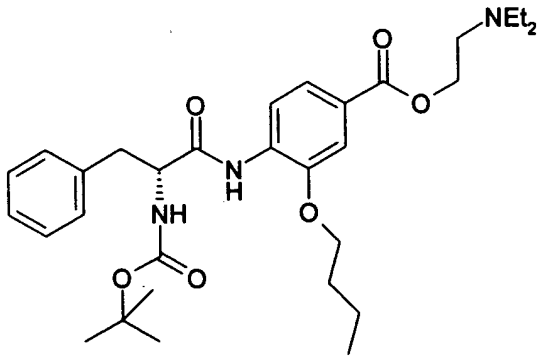

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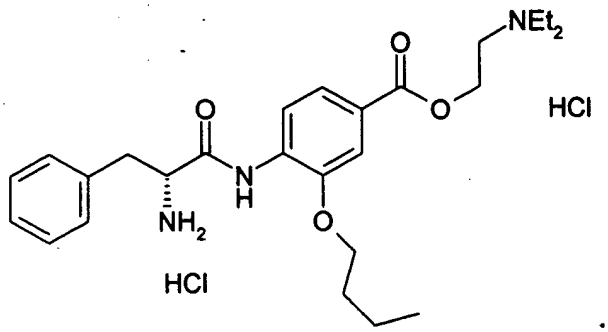
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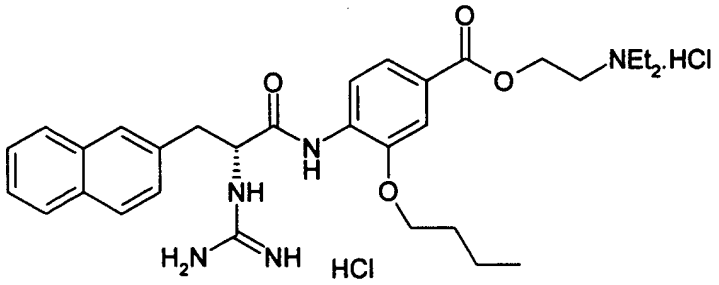
O
O
HCl
O
N
H
NH2
O
HCl

;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O
N
H
NH
O
H2N
NH
HCl

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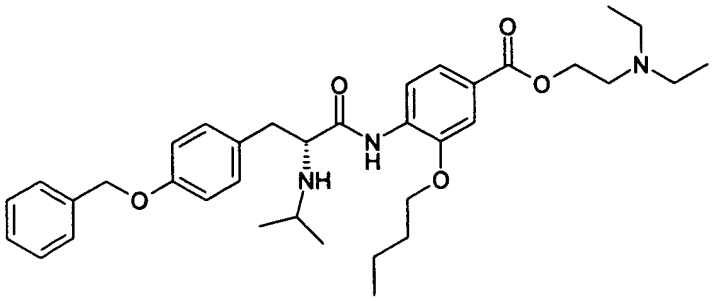
O
O
N
O
N
H
NH
O

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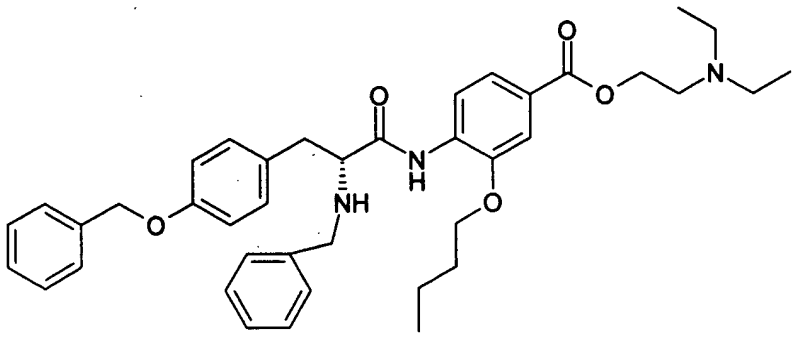
O
O
N
O
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NH
O

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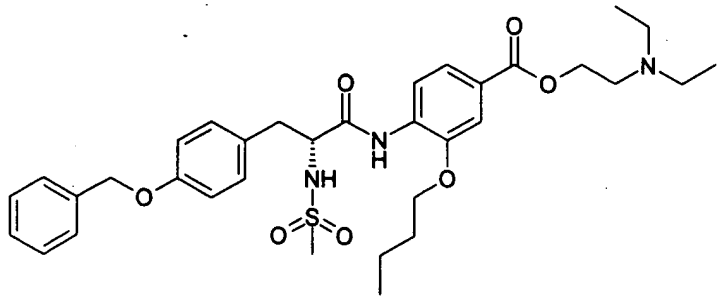

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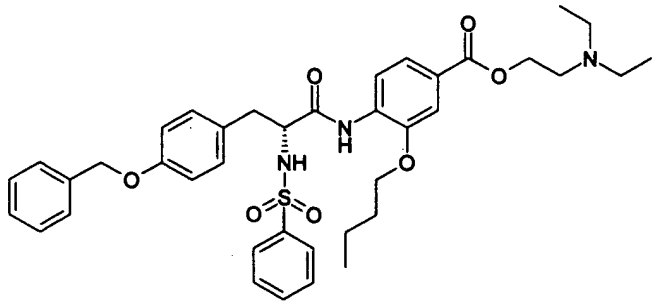

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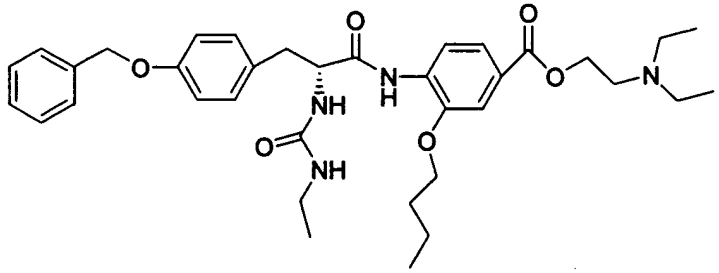

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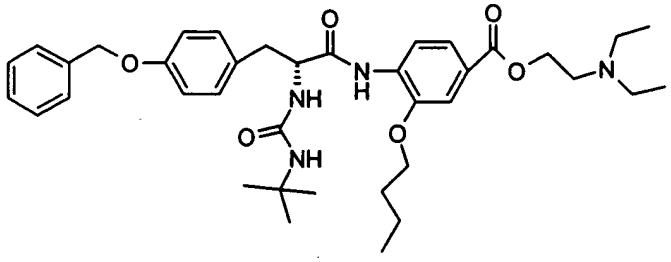

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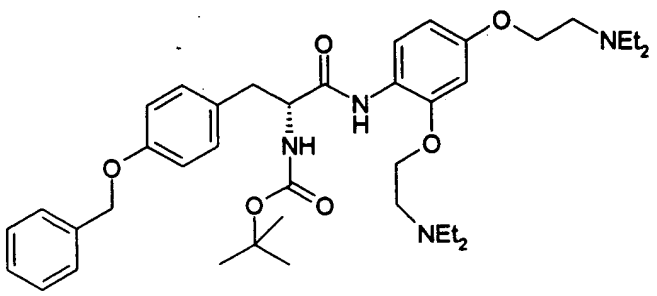

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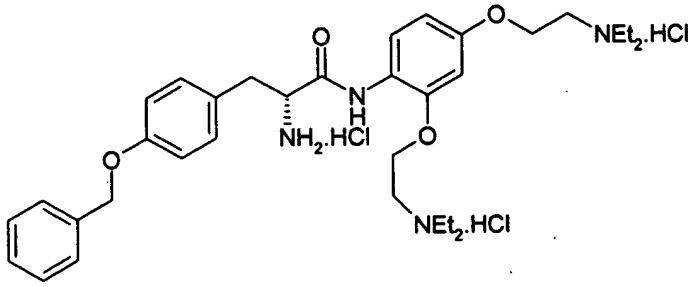

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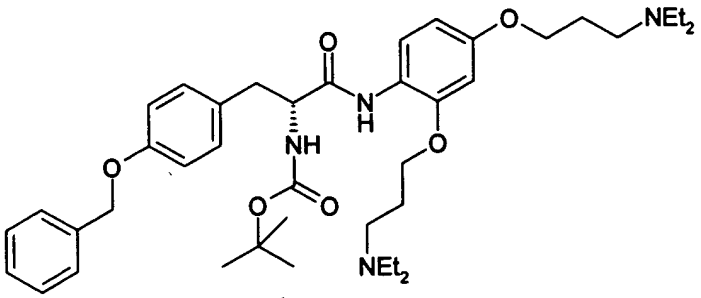

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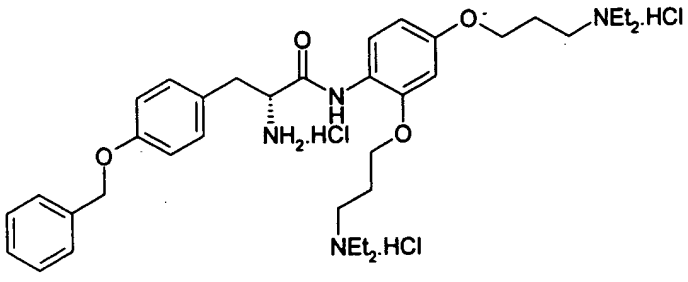

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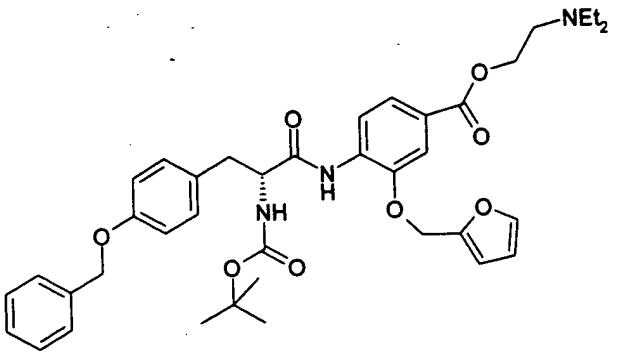
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NH
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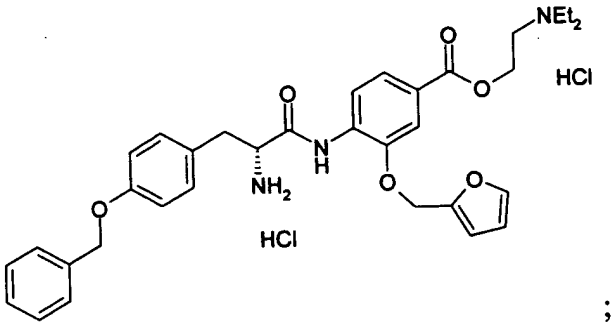
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HCl
O
O
O
N
H
NH2
HCl
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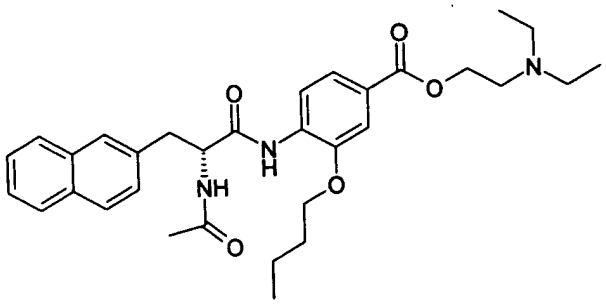
O

;


O
O
N
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NH
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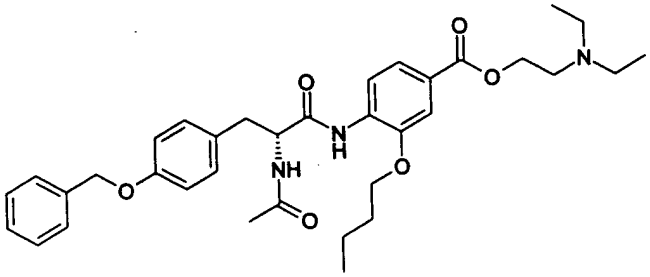
O

; and


O
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NH
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O

;

or the free amine, free acid, solvate, prodrug, or pharmaceutically acceptable salt thereof.

24. The pharmaceutical composition of claim 16, in the form of an oral dosage or parenteral dosage unit.

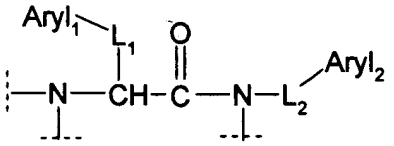
25. The pharmaceutical composition of claim 16, wherein said compound is administered as a dose in a range from about 0.01 to 500 mg/kg of body weight per day.

26. The pharmaceutical composition of claim 16, wherein said compound is administered as a dose in a range from about 0.1 to 200 mg/kg of body weight per day.

27. The pharmaceutical composition of claim 16, wherein said compound is administered as a dose in a range from about 0.1 to 100 mg/kg of body weight per day.

28. The pharmaceutical composition of claim 16, further comprising one or more therapeutic agents selected from the group consisting of alkylating agents, antimetabolites, plant alkaloids, antibiotics, hormones, biologic response modifiers, analgesics, NSAIDs, DMARDs, glucocorticoids, sulfonylureas, biguanides, insulin, cholinesterase inhibitors, antipsychotics, antidepressants, and anticonvulsants.

29. A method for the inhibition of the interaction of RAGE with its physiological ligands, which comprises administering to a subject in need thereof, at least one compound comprising at least one moiety of the formula

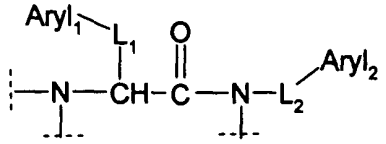


wherein L_1 and L_2 are each a hydrocarbon group of from 1 to 6 carbons or a direct bond, and $Aryl_1$ and $Aryl_2$ are aryl, wherein each of $Aryl_1$ and $Aryl_2$ are substituted by at least one lipophilic group.

30. The method of claim 29, wherein the ligand(s) is(are) selected from advanced glycated end products (AGEs), S100/calgranulin/EN-RAGE, β-amyloid and amphoterin.

31. A method for the inhibition of the interaction of RAGE with its physiological ligands, which comprises administering to a subject in need thereof, at least one compound of Formula (I) as claimed in claim 3.

32. A method for treating a disease state selected from the group consisting of acute and chronic inflammation, symptoms of diabetes, vascular permeability, nephropathy, atherosclerosis, retinopathy, Alzheimer's disease, erectile dysfunction, and tumor invasion and/or metastasis, which comprises administering to a subject in need thereof a therapeutically effective amount of at least one compound comprising at least one moiety of the formula



wherein L_1 and L_2 are each a hydrocarbon group of from 1 to 6 carbons, or a direct bond, and $Aryl_1$ and $Aryl_2$ are aryl, wherein each of $Aryl_1$ and $Aryl_2$ are substituted by at least one lipophilic group.

33. The method of claim 32, further comprising administering to a subject in need thereof at least one adjuvant and/or additional therapeutic agent(s).

34. A method of prevention and/or treatment of RAGE mediated human diseases, treatment comprising alleviation of one or more symptoms resulting from that disorder, to an outright cure for that particular disorder or prevention of the onset of the disorder, the method comprising administration to a human in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

35. A method for treating acute and/or chronic inflammation, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

36. A method for treating vascular permeability, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

37. A method for treating nephropathy, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

38. A method for treating atherosclerosis, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

39. A method for treating retinopathy, which comprises administering to a subject in need thereof a therapeutically effective amount of compound of Formula (I) as claimed in claim 3.

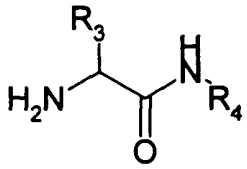
40. A method for treating Alzheimer's disease, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

41. A method for treating erectile dysfunction, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

42. A method for treating tumor invasion and/or metastasis, which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3.

43. A method of treating RAGE mediated diseases, the method comprising administering to a subject in need thereof, a therapeutically effective amount of a compound of Formula (I) as claimed in claim 3, in combination with one or more therapeutic agents selected from the group consisting of alkylating agents, antimetabolites, plant alkaloids, antibiotics, hormones, biologic response modifiers, analgesics, NSAIDs, DMARDs, glucocorticoids, sulfonylureas, biguanides, insulin, cholinesterase inhibitors, antipsychotics, antidepressants, and anticonvulsants.

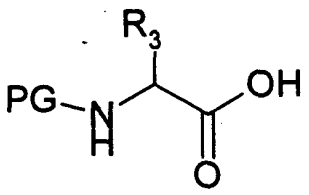
44. A process for preparing a compound of the Formula (II)



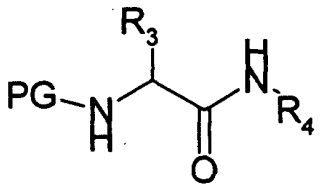
(II)

which comprises the steps:

(a) reacting a compound of the formula



with an amine of the formula R_4-NH_2, in the presence of a coupling reagent to form a compound of the formula



followed by removal of the protecting group PG,

wherein R_3 is selected from

a) -C_{1-6} alkyl;

b) –aryl; and

c) -C_{1-6} alkylaryl;

R_4 is selected from

a) -C_{1-6} alkylaryl;

b) -C_{1-6} alkoxyaryl; and

c) –aryl;

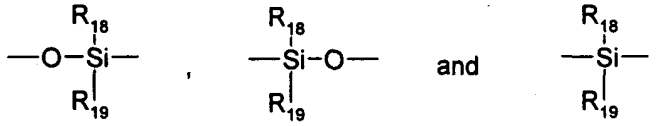
and wherein

the aryl and/or alkyl group(s) in R_3 and R_4 may be optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y- C_{1-6} alkyl;
-Y-aryl;
-Y-C_{-1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of -CH_2-, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -$NHSO_2$NH-, -O-CO-,



and

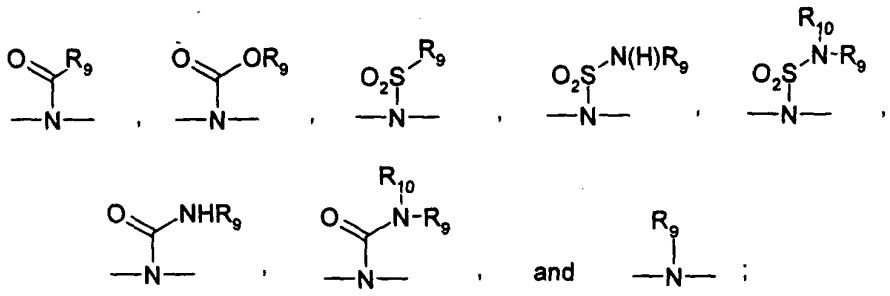
c) halogen, hydroxyl, cyano, carbamoyl, or carboxyl; and

R_{18} and R_{19} are selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl;

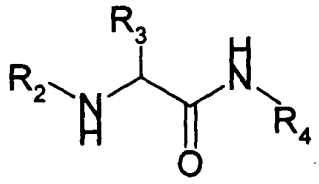
R_7 and R_8 are selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl; and wherein

R_7 and R_8 may be taken together to form a ring having the formula -$(CH_2)_m$-X-$(CH_2)_n$- bonded to the nitrogen atom to which R_7 and R_8 are attached, wherein m and n are, independently, 1, 2, 3, or 4; X is –CH_2-, -O-, -S-, -$S(O_2)$-, -C(O)-, -CON(H)-, -NHC(O)-, -NHCON(H)-, -$NHSO_2$-, -SO_2N(H)-, -C(O)-O-, -O-C(O)-, -$NHSO_2$NH-,



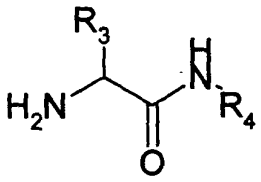
and PG is an amino protecting group.

45. A process for preparing a compound of Formula (III)



(III)

which comprises reacting a compound of Formula (II)



(II)

(A) with an aldehyde or ketone of the formula $R_{12}C(O)R_{11}$ in the presence of a reducing agent, wherein R_{12} and R_{11} are independently selected from

a) –H;

b) -C_{1-6} alkyl;

c) –aryl;

d) -C_{1-6} alkylaryl;

e) -C(O)-O-C_{1-6} alkyl;

f) -C(O)-O-C_{1-6} alkylaryl;

g) -C(O)-NH-C_{1-6} alkyl;

h) -C(O)-NH-C_{1-6} alkylaryl;

i) -SO_2-C_{1-6} alkyl;

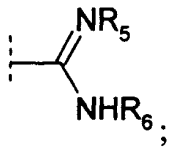
j) -SO_2-C_{1-6} alkylaryl;

k) -SO_2-aryl;

l) -SO_2-NH-C_{1-6} alkyl;

m) -SO_2-NH-C_{1-6} alkylaryl;

n)



;

o) -C(O)-C_{1-6} alkyl; and

p) -C(O)-C_{1-6} alkylaryl;

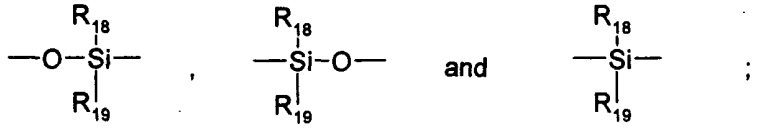
and wherein

the aryl and/or alkyl group(s) in R_1 and R_2 may be optionally substituted 1-4 times with a substituent group, wherein said substituent group(s) or the term substituted refers to groups selected from the group consisting of:

a) -H;

b) -Y-C_{1-6} alkyl;
-Y-aryl;
-Y-C_{-1-6} alkylaryl;
-Y-C_{1-6}-alkyl-NR_7R_8; and
-Y-C_{1-6}-alkyl-W-R_{20};

wherein Y and W are, independently selected from the group consisting of $-CH_2-$, -O-, -N(H), -S-, SO_2-, -CON(H)-, -NHC(O)-, -NHCON(H)-, $-NHSO_2-$, $-SO_2N(H)-$, -C(O)-O-, $-NHSO_2NH-$, -O-CO-,



and

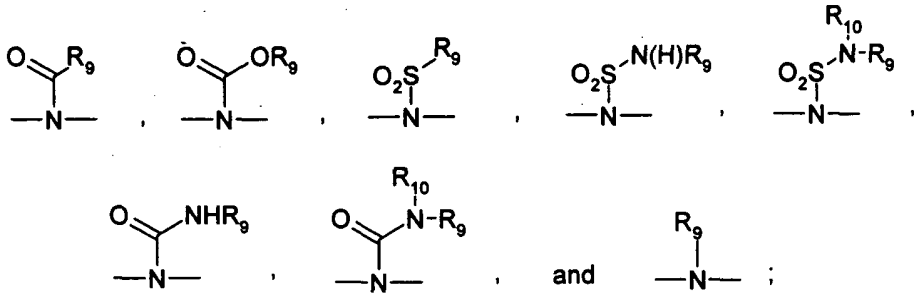
c) halogen, hydroxyl, cyano, carbamoyl, or carboxyl; and

R_7 and R_8 are selected from the group consisting of hydrogen, aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl;

R_{18} and R_{19} are selected from the group consisting of aryl, C_1-C_6 alkyl, C_1-C_6 alkylaryl, C_1-C_6 alkoxy, and C_1-C_6 alkoxyaryl;

R_{20} is selected from the group consisting of aryl, C_1-C_6 alkyl, and C_1-C_6 alkylaryl; and wherein

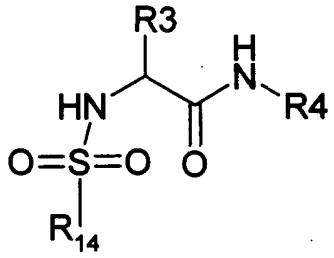
R_7 and R_8 may be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atom to which R_7 and R_8 are attached, and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula $-(CH_2)_m-X-(CH_2)_n-$ bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m and n are, independently, 1, 2, 3, or 4; X is $-CH_2-$, -O-, -S-, $-S(O_2)-$, -C(O)-, -CON(H)-, -NHC(O)-, -NHCON(H)-, $-NHSO_2-$, $-SO_2N(H)-$, -C(O)-O-, -O-C(O)-, $-NHSO_2NH-$,



or

(B) with a tertiary amine base and an alkylating agent of the formula R_2-Z, wherein Z is a nucleofugal group, and R_2 is as defined above for R_{12} or R_{11}.

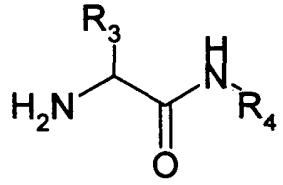
46. A process for preparing a compound of Formula (IV)



(IV)

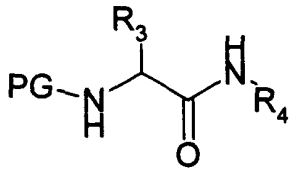
which comprises either

(a) treating a compound of the formula



with a compound of the formula $R_{14}SO_2Cl$, wherein R_{14} is C_{1-6} alkyl, C_{1-6} alkylaryl, or aryl, or

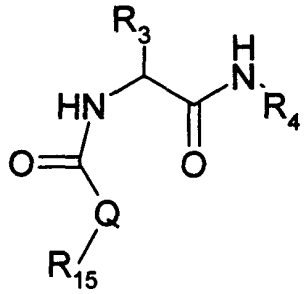
(b) treating an amine compound of the formula R_{15}-NH_2 with sulfuryl chloride, to afford an intermediate which is then contacted with a compound of the formula



;

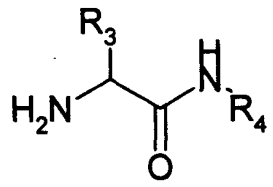
wherein R_3, R_4, and PG are as defined in claim 44.

47. A process for preparing a compound of Formula (V)



(V)

which comprises contacting a compound of Formula (II)

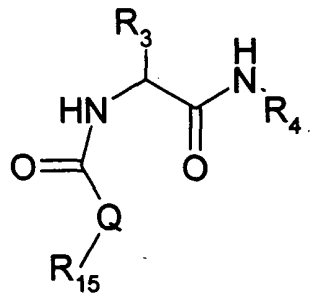


(II)

wherein R_3 and R_4 are as defined in claim 44,

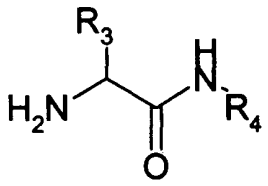
with a compound of the formula $R_{15}NCO$, optionally in the presence of a tertiary amine, wherein R_{15} is $-C_{1-6}$ alkyl or $-C_{1-6}$ alkylaryl and Q is –NH-.

48. A process for preparing a compound of Formula (V)



(V)

which comprises contacting a compound of Formula (II)

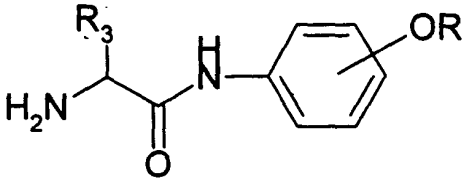


(II)

as defined in claim 47,

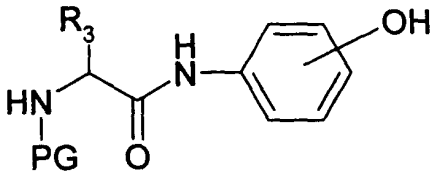
with a compound of the formula $R_{15}O$-C(O)Cl and a tertiary amine base, wherein R_{14} is $-C_{1-6}$ alkyl or $-C_{1-6}$ alkylaryl and Q is –O-.

49. A process for preparing a compound of Formula (VI)



(VI)

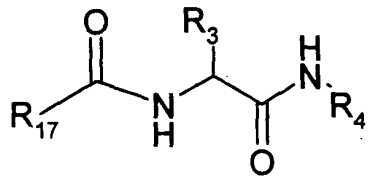
which comprises contacting a compound of the formula



with triphenylphosphine and either (a) diisopropyl azodicarboxylate or diethy azodicarboxylate and an alcohol of the formula $R_{16}OH$, followed by treatment with a strong base or strong acid, depending upon the identity of PG;

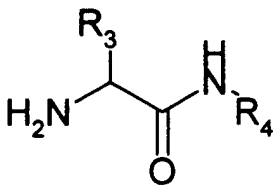
wherein PG is a urethane-type blocking group; and
R_{16} is C_{1-6} alkyl, -C_{1-6} alkylaryl, -C_{1-6} alkyl-Si(C_{1-6} alkyl)$_3$, -C_{1-6} alkyl-OSi(C_{1-6} alkylaryl)$_3$, or –C_{1-6} alkyl-NR_7R_8, provided that neither of R_7 and R_8 are hydrogen.

50. A process for preparing a compound of Formula (VII)



(VII)

which comprises contacting a compound of the formula



with either

(a) a compound of the formula $(R_{17}\text{-}CO)_2O$, in the presence of a tertiary amine;

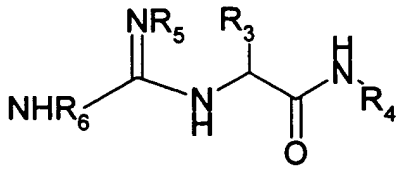
(b) a compound of the formula $R_{17}\text{-}C(O)Cl$, in the presence of a tertiary amine;

or

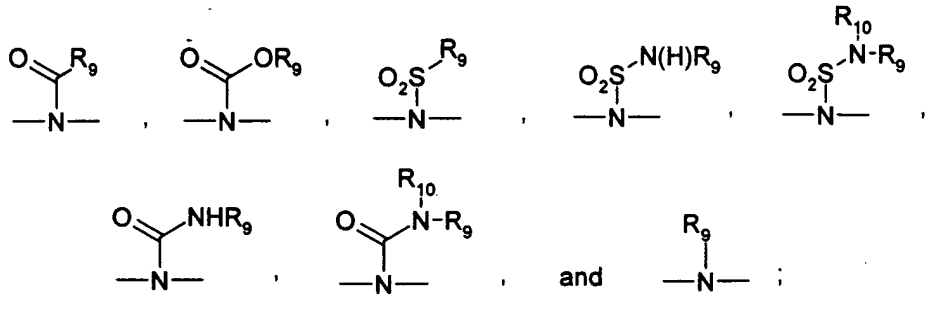
(c) a compound of the formula $R_{17}\text{-}C(O)OH$ and a coupling reagent.

wherein R_{17} is $C_{1\text{-}6}$ alkyl or $C_{1\text{-}6}$ alkylaryl; and R_3 and R_4 are as defined in claim 44.

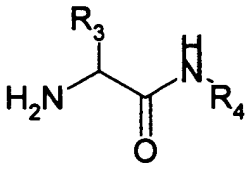
51. A process for preparing a compound of Formula (VIII)



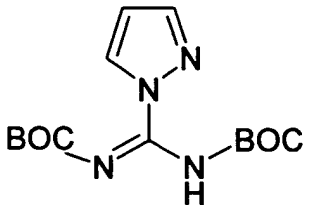
wherein R_3 and R_4 are as defined in claim 43, and R_5 and R_6 are independently selected from the group consisting of hydrogen, $C_1\text{-}C_6$ alkyl, $C_1\text{-}C_6$ alkylaryl, and aryl; and/or R_5 and R_6 may, independently, be taken together to form a ring having the formula $-(CH_2)_m\text{-}X\text{-}(CH_2)_n-$ bonded to the nitrogen atoms to which R_5 and R_6 are attached, wherein m and n are, independently, 1, 2, 3, or 4; X is selected from the group consisting of $-CH_2-$, -O-, -S-, $-S(O_2)-$, -C(O)-, -CON(H)-, -NHC(O)-, -NHCON(H)-, $-NHSO_2-$, $-SO_2N(H)-$, -C(O)-O-, -O-C(O)-, $-NHSO_2NH-$,



which comprises contacting a compound of the formula



with an activated amidine reagent of the formula



in the presence of a tertiary amine, followed by treatment with a strong acid, wherein BOC represents tert-butoxycarbonyl-.